REMARKS

Applicants have carefully considered the Examiner's comments in the Office Action dated March 19, 2003, and respond as follows.

Applicants have amended claim 1; in the last Office Action, this claim was amended to include the word "having". In writing the amended claims, Applicants erroneously deleted the term "β" to recite "a therapeutically effective amount of an RAR antagonist" rather than "a therapeutically effective amount of an RAR β antagonist". This error has now been corrected; Applicants regret any inconvenience caused by this error. Applicants have also made clear that the RAR antagonist is not specific to at least one other RAR receptor subtype. N Support for this amendment can be found on, e.g., page 5, lines 1-16.

Applicants again note that the Examiner has characterized the currently pending claims as constituting both method and composition claims. In fact, the pending claims are solely drawn to methods using an RARβ antagonist having specific RAR modulating activity. There are no composition claims currently pending.

Rejections Pursuant to 35 USC §112(1)

The Examiner has rejected claims 13-28, alleging that the pending method claims are not enabled by the specification to that a person of ordinary skill in the art could make or use them.

In support of her position, the Examiner has cited factors set forth in *Ex parte Forman*, 230 USPQ546 (Bd. Pat. App. & Int. 1986) and later cited in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) in an attempt to establish that compounds that are RAR specific and have RARβ antagonist activity (i.e., those used in the claimed methods) can only be found through undue experimentation.

Interestingly, the Examiner concedes that the RAR antagonists disclosed in the patents incorporated by reference within this application are enabled. October 31, 2002 Office Action at page 2. Such compounds constitute many thousands of structurally diverse compounds, including: aryl-and heteroarylcyclohexenyl substituted alkenes, benzo 1,2-chrom-3-ene and benzo1,2-thiochrom-3-ene compounds, N-aryl substituted tetrahydroquinolines, and aryl-substituted and aryl and (3-oxo-1-propenyl)-substituted benzopyran, benzothiopyran, 1,2-dihydroquinoline, and 5,6-dihydronaphthalene derivatives. Additionally, and as pointed out in past replies to Office Actions, screening methods for finding those antagonists that inhibit RARβ, such as the

transactivation assay described on page 13, lines 9 et seq., are also described in detail in the patents incorporated by reference (see, for example, US Patent 5,877,207, column 107, lines 12-59). Those of ordinary skill in the art clearly know that it is merely a matter of routine to test panels of compounds in assays such as the transactivation assay, which are amenable to high throughput computerized use. Such does the present patent application disclose in light of the state of the art known to the ordinary skilled artisan.

Nevertheless, the Examiner states that "the only compounds that are enabled by the instant specification have already been patented". With respect, Applicants submit that, to the extent this is true, it is irrelevant to the currently pending method claims. Applicants fully agree that the prior art discloses RAR β antagonists. Indeed, it is precisely this fact that helps enable the present invention. However, it is a misconception of the patent law to state that a new method of using a compound requires that the compound itself be new. To this end, Applicants again note that a "new use" is statutory subject matter under 35 USC §101, whether the materials used in it are old or not.

The Examiner agrees that the screening method is routine, but states that the compounds to test in the screening method are not. However, the specification enables the synthesis of those thousands of compounds disclosed in the patents cited and incorporated as part of this specification. Those having RAR β antagonist activity would clearly be the obvious starting point for synthesizing modifications of a core structure (so-called structure-activity relationship studies or SAR) – a process which has formed the basis for medicinal chemistry for decades. Many of these modifications are themselves directly and specifically enabled by the patent disclosures incorporated by reference herein. For those that are not, modified compounds can be synthesized using well known synthetic methods or compound libraries can be commercially purchased for screening.

Because the prior art (including that expressly incorporated by reference herein) discloses a vast variety of β RAR antagonists, because methods of finding additional RAR β antagonists are routine in the art and because suitable methods of administration are both well known and described in the specification, the person of ordinary skill in the art would clearly be able to make and use the present invention without undue experimentation.

Rejection Pursuant to 35 USC 102(b)

The Examiner has rejected claims 13-28 as anticipated by each of Ghaffari, Cong, Xu, Wu, Co, Song,

and Yu. The Examiner argues that all these references "disclose RAR modulation and lung tissues". Applicants traverse these rejections.

In order to anticipate, a single reference must contain, either literally or implicitly, each and every limitation of the claim at issue. See e.g., *In re Paulson*, 31 USPQ2d 1671 (Fed. Cir. 1994). The Examiner has not shown that any of the references disclose a method for the treatment or prevention of alveolar destruction by using an RAR-specific RAR β antagonist. Additionally, Applicants have found no such disclosure in any of these references. If the Examiner has found an anticipatory disclosure of each and every limitation of any of the present claims in one or more of these references, Applicants respectfully request the Examiner to expressly point to such disclosure.

CONCLUSION

For these reasons, Applicants respectfully submit that the claims are in condition for allowance, and respectfully request that the Examiner issue a Notice to that effect. Should any fees (such as an extension of the time to reply) be due in with this Reply, please use our Deposit Account No. 01-0885.

Respectfully submitted,

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